Complete Summary

GUIDELINE TITLE

Rituximab in lymphoma and chronic lymphocytic leukemia: a clinical guideline

BIBLIOGRAPHIC SOURCE(S)

Hematology Disease Site Group. Imrie K, Stevens A, Meyer R. Rituximab in lymphoma and chronic lymphocytic leukemia: a clinical practice guideline. Toronto (ON): Cancer Care Ontario (CCO); 2005 Feb 17. 43 p. (Evidence-based series; no. 6-8). [51 references]

GUIDELINE STATUS

This is the current release of the guideline.

The Guideline will expand over time to contain new information emerging from their reviewing and updating activities.

Please visit the <u>Cancer Care Ontario Web site</u> for details on any new evidence that has emerged and implications to the guidelines.

COMPLETE SUMMARY CONTENT

SCOPE

METHODOLOGY - including Rating Scheme and Cost Analysis RECOMMENDATIONS

EVIDENCE SUPPORTING THE RECOMMENDATIONS

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

QUALIFYING STATEMENTS

IMPLEMENTATION OF THE GUIDELINE

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT

IDENTIFYING INFORMATION AND AVAILABILITY

DISCLAIMER

SCOPE

DISEASE/CONDITION(S)

Lymphoma and chronic lymphocytic leukemia

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness Treatment

CLINICAL SPECIALTY

Hematology Oncology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

Lymphoma

- To evaluate if rituximab used alone or in combination with chemotherapy is more effective than non-rituximab-containing regimens for improving overall survival, disease control (as assessed by measures such as progression-free survival, event-free survival, time-to-treatment failure, or response duration), response rate, or quality of life in patients with lymphoma of any type or stage
- To evaluate the toxicity associated with the use of rituximab used alone or in combination with chemotherapy compared with non-rituximab-containing regimens
- To evaluate which patients with lymphoma are more or less likely to benefit from treatment with rituximab compared with those treated with non-rituximab--containing regimens

Chronic Lymphocytic Leukemia (CLL)

- To evaluate what beneficial outcomes are associated with the use of rituximab for the treatment of patients with chronic lymphocytic leukemia
- To evaluate the toxicity associated with the use of rituximab
- To evaluate which patients are more or less likely to benefit from treatment with rituximab

TARGET POPULATION

Lymphoma

Adult patients with lymphoma of any type, at any stage, and any histology

Chronic Lymphocytic Leukemia (CLL)

Adult patients with chronic lymphocytic leukemia at any stage

INTERVENTIONS AND PRACTICES CONSIDERED

Treatment

Rituximab monotherapy or combination therapy versus non-rituximab regimens

MAJOR OUTCOMES CONSIDERED

- Overall survival
- Disease control, as assessed by measures such as:
 - Progression-free survival
 - Event-free survival
 - Time to treatment failure
 - Response duration
- Response rate
- Quality of life
- Toxicity of rituximab alone or in combination with chemotherapy

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources) Hand-searches of Published Literature (Secondary Sources) Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Lymphoma

MEDLINE® In-Process & Other Non-Indexed Citations (Ovid) (December 12, 2003), MEDLINE (Ovid) (1966 through November 2003), HealthStar (Ovid) (1975 through November 2003, limited to nonMEDLINE), CINAHL (Ovid) (1982 through December 2003), and the Cochrane Library (2003, Issue 4) databases were searched. In MEDLINE, "Exp lymphoma/" (Medical subject heading [MeSH]) was combined with "exp lymphoma, large-cell/" (MeSH), "lymphoma.mp." (textword), and each of the following phrases used as text words: "rituxan.mp.," "rituximab.mp.," "ritux:.mp.," "idec.mp." combined with "c2b8.mp." or "c2b?.mp.," "anti -cd20.mp.," "anticd-20.mp.," "anticd20.mp.," "mabthera.mp.," and "rituxin.mp.". These terms were then combined with the search terms for the following publication types and study designs: practice guidelines, systematic reviews, meta-analyses, reviews, randomized controlled trials, controlled clinical trials, and clinical trials. Searches in the other bibliographic databases were similar. The MEDLINE search focused on retrieving randomized controlled trials.

In addition, conference proceedings of American Society of Hematologists (ASH) (1998-2003) and the American Society of Clinical Oncology (ASCO; 1997-2003) were searched for abstracts of relevant trials. Personal files were also consulted.

Relevant bibliographic citations were selected by two reviewers. All the evidence was reviewed by two reviewers.

Chronic Lymphocytic Leukemia (CLL)

MEDLINE (Ovid) (1966 through December 2002), MEDLINE® In-Process & Other Non-Indexed Citations (Ovid) (January 10, 2003), CANCERLIT (Ovid) (1975 through October 2002, limited to nonMEDLINE), HealthStar (OVID) (1975 through

October 2002, limited to nonMEDLINE), CINAHL (1982 through December 2002), and the Cochrane Library (Ovid) (2002, Issue 4; the Cochrane Central Register of Controlled Trials and Cochrane Database of Systematic Reviews were searched) databases were searched. In MEDLINE, "Leukemia, lymphocytic/" (MeSH) was combined with "exp leukemia, lymphocytic, chronic/" (MeSH), "chronic lymphocytic leukemia.mp." (textword), "chronic lymphocytic leukaemia.mp.," "CLL.mp.," and each of the following phrases used as textwords: "rituxan.mp.," "rituximab.mp.," "ritux:.mp.," "idec.mp." combined with "c2b8.mp." or "c2b?.mp.," "anti -cd20.mp.," "anticd-20.mp.," "anticd20.mp.," and "mabthera.mp.". Searches in the other bibliographic databases were similar.

In addition, conference proceedings of American Society of Hematologists (1996-2003) and American Society of Clinical Oncology (1995-2003) were searched for abstracts of relevant trials. The Canadian Medical Association Infobase (http://mdm.ca/cpgsnew/cpgs/index.asp) and the National Guideline Clearinghouse (http://www.guideline.gov) were also searched for existing evidence -based practice guidelines. Personal files were also reviewed.

Relevant bibliographic citations were selected by two reviewers in the original literature search. Evidence was reviewed by two reviewers.

Study Selection Criteria

Inclusion Criteria

Lymphoma

Articles were selected for inclusion in this systematic review of the evidence if they were fully published reports or published abstracts in the English language of:

- 1. Randomized controlled trials, systematic reviews, meta-analyses, or evidence-based practice guidelines
- 2. Studies that include adult patients with lymphoma of any type, at any stage, and any histology
- 3. Studies comparing rituximab alone with non-rituximab regimens or comparing rituximab combination therapy with non-rituximab regimens
- 4. Studies evaluating one or more of the following outcomes: overall survival, disease control (progression-free survival, event-free survival, time-to-treatment failure, or response duration), response rate, quality of life, or toxicity.

CLL

Articles were selected for inclusion in this systematic review of the evidence if they were fully published reports or published abstracts in the English language of:

1. Primary studies of any design type, systematic reviews, meta-analyses, or evidence-based clinical practice guidelines

- 2. Studies that include patients with CLL or small lymphocytic lymphoma (SLL). For studies including patients with various histologic subtypes of lymphoproliferative disorders, outcomes of patients with CLL must be identified separately
- 3. Studies evaluating rituximab alone or in combination with other agents
- 4. Studies evaluating at least one of the following outcomes were reported: overall survival, disease control (progression-free survival, time-to-treatment failure, event-free survival, or response duration), or toxicity. If response rate is reported, at least one of the above outcomes must also be reported to be included.

Exclusion Criteria

Lymphoma

Letters, comments, books, notes, and editorial publication types were not considered.

CLL

The following were not considered:

- 1. Letters, comments, and editorial publication types.
- 2. Reports evaluating patients undergoing stem cell transplantation.
- 3. Studies with fewer than 10 patients.

Article Selection

Lymphoma

Citations were reviewed by two reviewers for inclusion. Citations were not blinded for author, journal name, institution, or results. Each citation was scored as: "Yes" (inclusion criteria were met, no exclusion criteria were met), "No" (one or more exclusion criteria were met), or "Maybe" (unclear from the citation if article meets any criteria). The full-length article was retrieved if the citation was scored "yes" or "maybe" by at least one reviewer, and inclusion and exclusion criteria were applied to the full article, if necessary. Inter-observer kappa coefficients were calculated using GraphPad QuickCalcs © (GraphPad Software, Inc.) (http://graphpad.com/quickcalcs/kappa1.cfm).

CLL

Citations in the original literature search were reviewed by two reviewers for inclusion. Citations were not blinded for author, journal name, institution, or results. Each citation was scored as: "Yes" (inclusion criteria were met, no exclusion criteria were met), "No" (one or more exclusion criteria were met), or "Maybe" (unclear from the citation if article meets any criteria). The full-length article was retrieved if the citation was scored "yes" or "maybe" by at least one reviewer, and inclusion and exclusion criteria were applied to the full article, if necessary. Interobserver kappa coefficients were calculated using GraphPad

QuickCalcs © (GraphPad Software, Inc.) (http://graphpad.com/quickcalcs/kappa1.cfm).

NUMBER OF SOURCE DOCUMENTS

Lymphoma

Twelve articles (11 trials) were eligible for inclusion and review.

Chronic Lymphocytic Leukemia

Twenty-seven articles (24 trials) were eligible for inclusion and review.

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus (Committee)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Study Quality Assessment

Lymphoma

Methodologic assessment could not be performed as most of the trials identified were reported in abstract form only and insufficient information was available for detailed assessment. Assessment using the Jadad quality assessment tool was performed for fully published reports.

Chronic Lymphocytic Leukemia

No reports were evaluated with the Jadad quality assessment tool as no randomized trials were identified.

Synthesizing the Evidence

Lymphoma

The Disease Site Group (DSG) identified that a meta -analysis of the published evidence for this topic is a high priority. However, sufficient information to allow for a meta-analysis is currently unavailable in the published abstracts. The authors will consider conducting a meta-analysis in a future update of this

guideline using Review Manager 4.2 (RevMan Analyses), which is available through the Cochrane Collaboration.

Chronic Lymphocytic Leukemia

Data appropriate for meta-analysis were not identified.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

In evaluating the evidence assessing rituximab for the treatment of patients with lymphoproliferative disorders, the Hematology Disease Site Group (DSG) developed a series of principles, summarized below, that were applied to their deliberations.

The Role of Randomized Trials

Given the potential for bias associated with non-randomized comparative trials, the Hematology DSG has limited its assessment to randomized controlled trials. However, the lack of available randomized trials assessing rituximab in patients with chronic lymphocytic leukemia (CLL) limits the ability to assess whether rituximab provides a benefit to these patients.

Influence of Disease Histology

The clinical behaviour and management of patients with various histologic types of lymphoma is known to differ among the types. These differences in behaviour can influence the interpretation of outcome measures used in clinical trials that evaluate new therapies.

Generalizability of Results

The clinical trials evaluating rituximab have assessed specific patient populations and have used criteria such as histology, patient age, stage, number of prognostic risk factors, and amount of previous therapy to define eligibility for entry into the respective clinical trials.

Limitations Associated with Publications in Abstract Form

The publication of data in abstract form imposes important limitations on the evaluation of those data: a detailed appraisal of trial methodology and the evaluation of all relevant outcomes are often not possible. Balanced against these limitations is the risk of not incorporating new data into practice when the data demonstrate a clear benefit, or incorporating it when the data demonstrate a clear harm, associated with a therapy.

Diffuse Large Cell Lymphoma

Based on the consistency of the results of the two studies testing the addition of rituximab to cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) in older patients, the Disease Site Group (DSG) concluded that the current recommendation to combine rituximab with CHOP when treating older patients with diffuse large B-cell lymphoma (DLBCL) should be maintained. The main point of debate among DSG members related to the role of rituximab in patients less than age 60 years. The DSG members acknowledged that there are no published randomized trials specifically studying the addition of rituximab to chemotherapy in younger patients. However, with the confirmation by Habermann et al that the duration of disease control is superior with rituximab, the DSG concluded that the results observed in older patients should be generalized to younger patients (age less than 60 years) who have this disease.

The role of rituximab for patients who present with limited-stage DLBCL was also discussed. These patients are commonly treated with abbreviated chemotherapy and involved field radiation. None of the published trials tested rituximab in addition to combined modality therapy. However, the DSG concluded that, in the absence of direct evidence evaluating this patient group, the results of the trials in advanced stage disease should be generalized to this population.

The treatment of DLBCL that has transformed from an indolent lymphoma was also discussed. While these patients were excluded from the published trials, the DSG concluded that, as the addition of rituximab to chemotherapy improved disease control for patients with follicular and other indolent lymphomas and for patients with DLBCL, the results of those trials should be generalized to patients with transformed lymphoma. The DSG therefore recommended that patients with transformed lymphoma who have not previously received treatment for the transformed disease, have not previously received rituximab, and who otherwise are appropriate candidates to receive CHOP, should receive rituximab in combination with CHOP.

The DSG concluded that there are insufficient data to support using rituximab in patients with HIV-related lymphoma. Potential differences in the disease process of this form of lymphoma and the greater risk of infections preclude generalizing data derived in non-HIV patients to this population.

Follicular and Other Low-Grade Lymphomas

The three trials comparing rituximab-containing regimens to chemotherapy without rituximab demonstrated a substantial improvement in disease control without an increase in major toxicity; an improvement in overall survival was observed in the trial comparing fludarabine, cyclophosphamide, and mitoxantrone (FCM) with FCM plus rituximab in previously treated patients. Given that those results have been obtained in both previously treated and untreated patients, and that three different chemotherapy regimens were utilized, the DSG concluded that combining rituximab with any chemotherapy regimen that is considered standard when treating these patients would be a preferred option when treatment is required. The majority of the DSG favoured generalizing these results to other indolent lymphoma histologies (excluding chronic lymphocytic leukemia [CLL] and small lymphocytic lymphoma [SLL]).

The role of retreatment with rituximab was actively discussed by the DSG. Published trials demonstrating a benefit in disease control or overall survival with the addition of rituximab did not evaluate patients who had previously received rituximab. Therefore, the DSG concluded that there are currently insufficient data to support or refute the retreatment with rituximab of patients who have previously received the drug as either a single agent or as part of a combination therapy. The DSG is aware of the potential limitations of those data and this conclusion. As the results of all the trials have been reported in preliminary abstract form only, these conclusions will require review when the fully published trial results become available. The DSG members recognize that the re-use of therapies that have previously been successful in a given patient is standard practice in treating indolent lymphoma. The DSG anticipates that the issue of retreatment will require specific re-evaluation within the next two to three years and hope that further data addressing this point will eventually become available. If not, this issue may require re-evaluation to determine how more mature data published in article form might be generalized to the role of retreatment.

With respect to maintenance therapy, the DSG recognized that two trials reported superior disease control in patients receiving rituximab maintenance. In both trials, patients initially received rituximab monotherapy. In one trial, no ultimate improvement in disease control was observed with maintenance therapy in comparison with retreating patients with rituximab at disease progression; the second trial did not evaluate 'duration of rituximab benefit' as an outcome measure. The DSG concluded that those data were insufficient to support or refute a recommendation to use maintenance therapy.

Chronic Lymphocytic Leukemia

The data reviewed were considered to be insufficient to support or refute a recommendation to treat these patients with rituximab. The DSG also considered whether the data for treating patients with lymphoma could be generalized to those with CLL. As indicated in the original publication of Evidence Summary Report #6-8, rituximab appears to be associated with an inferior response rate in CLL in comparison with that seen when the drug is used as a single agent to treat patients with follicular and other low-grade lymphomas. The DSG concluded that the recommendations for using rituximab in patients with CLL would therefore require the results to be from randomized trials.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Based on the evidence and the draft recommendations, feedback was sought from Ontario clinicians. Practitioner feedback was obtained through a mailed survey of 120 practitioners in Ontario (60 hematologists, 30 academic medical oncologists, and 30 community medical oncologists). The survey consisted of items evaluating the methods, results, and interpretive summary used to inform the draft recommendations and whether the draft recommendations should be approved as a practice guideline. Written comments were invited. The practitioner feedback survey was mailed out on August 9, 2004. Follow-up reminders were sent at two weeks (post card) and four weeks (complete package mailed again).

The evidence-based series was circulated to members of the Practice Guidelines Coordinating Committee (PGCC) for review and approval. Eight of 13 members of the PGCC returned ballots. One of the eight members that returned ballots is a member of the Hematology DSG and was therefore not eligible to comment on the evidence -based series. Five members approved the evidence -based series as written, one member approved the guideline and provided suggestions for consideration by the Hematology DSG, and one member approved the guideline conditional on the Hematology DSG addressing specific concerns.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Lymphoma

- Previously untreated patients with diffuse large B-cell lymphoma (DLBCL), or a variant of DLBCL (such as mediastinal sclerosing B-cell lymphoma, T-cellrich B-cell lymphoma, Burkitt-like lymphoma, or intravascular lymphoma), who are candidates for treatment with curative intent and will receive cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP), should receive this therapy in combination with rituximab. This grouping includes patients with untreated DLBCL that has transformed from follicular or other indolent lymphoma. Rituximab should be administered at a dose of 375 milligrams (mg)/m² and given at the beginning of each treatment cycle of CHOP.
- There is insufficient evidence at this time to support or refute treatment with a rituximab-containing chemotherapy regimen in patients who have been previously treated for diffuse DLBCL or a variant of DLBCL.
- There is insufficient evidence to support combining rituximab with chemotherapy when treating patients with human immunodeficiency virus (HIV)-related lymphoma. These patients may be at an increased risk for life threatening infections when rituximab is combined with CHOP.
- Previously untreated patients with follicular or other indolent B-cell-histology lymphoma (such as mantle cell lymphoma, marginal zone lymphoma, and lymphoplasmacytoid lymphoma), excluding small lymphocytic lymphoma (SLL), who are appropriate candidates for chemotherapy, should receive this chemotherapy in combination with rituximab. Rituximab should be administered at a dose of 375 mg/m² and given at the beginning of each treatment cycle of chemotherapy.

- Previously treated patients with follicular or other indolent B-cell-histology lymphoma (such as mantle cell lymphoma, marginal zone lymphoma, and lymphoplasmacytoid lymphoma), excluding small lymphocytic lymphoma (SLL), who are appropriate candidates for chemotherapy and who have not previously received rituximab, should receive this chemotherapy in combination with rituximab. Rituximab should be administered at a dose of 375 mg/m² and given at the beginning of each treatment cycle of chemotherapy.
- There is currently insufficient evidence to support or refute the additional use of rituximab as a maintenance therapy in patients who have completed chemotherapy plus rituximab.
- There is insufficient evidence at this time to support or refute retreatment with a rituximab-containing chemotherapy regimen in patients who have previously received rituximab.

Chronic Lymphocytic Leukemia (CLL)

• There is insufficient evidence at this time to support or refute the use of single-agent rituximab or a rituximab-containing chemotherapy regimen in patients with chronic lymphocytic leukemia (CLL).

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The recommendations are supported by randomized controlled trials.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- In one randomized trial comparing cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) plus rituximab (CHOP-rituximab) with CHOP alone in previously untreated patients with diffuse large B-cell lymphoma (DLBCL) (aged 60 to 80 years), complete response, disease control (event-free survival), and overall survival were superior in patients allocated to receive CHOP-rituximab.
- In one randomized trial comparing CHOP-rituximab with CHOP alone, in previously untreated patients with diffuse large B-cell lymphoma (age 60 years and greater), disease control (time-to-treatment failure) was superior in patients allocated to receive CHOP-rituximab. No difference between randomized groups in overall survival was detected. In that trial, patients responding to induction therapy underwent a second randomization to receive maintenance therapy with rituximab or to be observed. Disease control (time-to-treatment failure) was superior in patients allocated to receive rituximab; no difference between randomized groups in overall survival was detected.

- In two trials comparing chemotherapy with or without rituximab in previously untreated patients with follicular lymphoma, disease control (time-to-treatment failure or time to progression) was superior in patients allocated to receive rituximab. Overall survival results were not reported for either trial.
- In one trial comparing chemotherapy with or without rituximab in previously treated patients with indolent lymphomas, response rate, disease control (progression-free survival) and overall survival were superior in patients allocated to receive rituximab.
- No important additional hematologic or non-hematologic toxicities were observed when rituximab was combined with chemotherapy.

POTENTIAL HARMS

Lymphoma

The authors have previously summarized treatment-related toxicity with singleagent rituximab; in general, this treatment is well tolerated with frequent, but rarely severe, infusional toxicities observed. The majority of adverse events occurred with the first infusion. While the availability of randomized trials now allow for a more detailed evaluation of toxicities, the details of toxicities are lacking in most of the preliminary abstract publications. In the randomized trial of cyclophosphamide, doxorubicin, vincristine, and prednisone plus rituximab (CHOP-R) compared with CHOP alone reported by Coiffier et al, no differences in hematologic toxicities were detected; an increase in grade 1 cardiac events, consistent with infusional toxicities, was observed in patients allocated to receive CHOP-R (24 vs. 13 percent, respectively; p-value not provided). The authors also report a non-significant trend towards more herpes zoster infections in patients receiving rituximab (nine vs. two patients, respectively; p=0.40). In addition to infusion-related toxicity similar to that described in the initial evidence summary. an increased incidence of a specific toxicity associated with rituximab use was reported in three publications: Hiddemann et al reported an increase in Grade III/IV neutropenia (42 vs. 37 percent; p-value not stated) and allergy-like symptoms (four vs. 0 percent; p-value not stated); Herold et al reported an increase in grade 4 leukopenia (13 vs. 6 percent; p=0.008); and Kaplan et al reported a higher incidence of deaths attributed to infection with CHOP-R than CHOP (14 vs. 2 percent, respectively; p=0.02) in patients with human immunodeficiency virus (HIV)-associated lymphoma.

Chronic Lymphocytic Leukemia

The chronic lymphocytic leukemia (CLL) monotherapy reports described toxicities that were similar to those previously summarized with single-agent rituximab. Again, treatment was well tolerated with frequent, but rarely severe, infusional toxicities observed. The majority of adverse events occurred with the first infusion. Winkler et al reported ten grade III/IV events (one grade IV) from the first infusion in three patients (30%); all three had high baseline peripheral lymphocyte counts (50 x 10^9 per litre or greater). After a massive cytokine-release syndrome with the first infusion in the first patient, subsequent patients with lymphocytes greater than 10×10^9 per litre received a fractionated schedule. Toxicity in combination therapy will be evaluable once randomized controlled trial data are available.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- Rituximab has a favourable single-agent toxicity profile. The addition of rituximab to chemotherapeutic regimens such as cyclophosphamide, vincristine, and prednisone (CVP), cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP), and fludarabine, cyclophosphamide, and mitoxantrone (FCM) does not appear to significantly alter the toxicity of these regimens in lymphoma.
- There is a rapid availability of new data regarding the role of rituximab in treating these diseases. Practitioners and patients are advised to review the Web site of Cancer Care Ontario's Program in Evidence-based Care (PEBC) to learn the status of this practice guideline.
- Care has been taken in the preparation of the information contained in this
 document. Nonetheless, any person seeking to apply or consult the practice
 guideline is expected to use independent medical judgment in the context of
 individual clinical circumstances or seek out the supervision of a qualified
 clinician. Cancer Care Ontario makes no representation or guarantees of any
 kind whatsoever regarding their content or use or application and disclaims
 any for their application or use in any way.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Hematology Disease Site Group. Imrie K, Stevens A, Meyer R. Rituximab in lymphoma and chronic lymphocytic leukemia: a clinical practice guideline. Toronto (ON): Cancer Care Ontario (CCO); 2005 Feb 17. 43 p. (Evidence-based series; no. 6-8). [51 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2005 Feb 17

GUI DELI NE DEVELOPER(S)

Program in Evidence-based Care - State/Local Government Agency [Non-U.S.]

GUI DELI NE DEVELOPER COMMENT

The Program in Evidence-based Care (PEBC) is a project supported by Cancer Care Ontario and the Ontario Ministry of Health and Long-Term Care.

SOURCE(S) OF FUNDING

Cancer Care Ontario
Ontario Ministry of Health and Long-Term Care

GUIDELINE COMMITTEE

Provincial Hematology Cancer Disease Site Group

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

For a current list of past and present members, please see the <u>Cancer Care Ontario Web site</u>.

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

The members of the Hematology Disease Site Group (DSG) disclosed potential conflicts of interest relating to the topic of this practice guideline. The lead author and citation and evidence reviewer (KI) of this topic was a co -investigator in one trial included in this report and is involved with an ongoing trial on rituximab. Three other DSG members reported research involvement with trials on this topic, of which one member was involved with one trial in this report. In addition, three of the above DSG members, including the lead author, reported involvement with the pharmaceutical company that manufactures rituximab, including research funding, membership on boards of directors or advisory committees, provision of consultancy, or honoraria.

GUIDELINE STATUS

This is the current release of the guideline.

The Guideline will expand over time to contain new information emerging from their reviewing and updating activities.

Please visit the <u>Cancer Care Ontario Web site</u> for details on any new evidence that has emerged and implications to the guidelines.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the <u>Cancer</u> Care Ontario Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Rituximab in lymphoma and chronic lymphocytic leukemia: a clinical practice guideline. Summary. Toronto (ON): Cancer Care Ontario (CCO). Electronic copies: Available in Portable Document Format (PDF) from the <u>Cancer Care</u> Ontario Web site.
- Browman GP, Levine MN, Mohide EA, Hayward RSA, Pritchard KI, Gafni A, et al. The practice guidelines development cycle: a conceptual tool for practice guidelines development and implementation. J Clin Oncol 1995;13(2):502-12.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on August 11, 2005. The information was verified by the guideline developer on September 16, 2005.

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